Our Dermatology Online

Case Report

Nicolau syndrome following injection of benzathine penicillin with neurological and muscular complications

Amond Stephen Anderson Kouabenan[1,2], Irénée Gué[1,2], Armel Mienwoley Oussou[1,2], Mityu Akanbi Sulé[1,2], Wilfried Koffi N'guessan[2], Almamy Diabaté[1,2]

[1]Department of Medicine, Alassane Ouattara University (Bouaké), Bouaké, Ivory Coast, [2]Dermatology Department, University Teaching Hospital of Bouaké, Bouaké, Ivory Coast

Corresponding author: Amond Stephen Anderson Kouabenan, MD, E-mail: stephandy2016@gmail.com

ABSTRACT

Nicolau syndrome is a rare adverse effect occurring after injections. The purpose of this observation was to report on a new case with a view to implementing preventive measures. A 32-year-old man consulted at the Dermatology Department of the Teaching Hospital of Bouaké for inflammatory swelling of the entire left lower limb following an intramuscular injection of 2.4 million international units of benzathine penicillin administered into the left thigh. Mucocutaneous examination revealed livedoid dermatitis of the left thigh associated with inflammatory swelling of the left lower limb. Neuromuscular examination revealed paresis of the entire left lower limb with contracture of the left quadriceps. CPK and LDH were elevated. The diagnosis of left Nicolau crural syndrome complicated by neurological and muscular damage was retained. Nicolau syndrome is an iatrogenic skin necrosis. Compliance with precautionary measures during injections is essential to limit its occurrence.

Key words: Benzathine penicillin, Paresis, Quadricipital contracture, Creatine phosphokinase, Lactic dehydrogenase

INTRODUCTION

Nicolau syndrome (NS) or drug-induced cutaneous embolism is an iatrogenic skin necrosis. It is a rare accident occurring during intramuscular, subcutaneous, intra-articular or intravenous injections [1,2]. The purpose of this study was to report a new case of Nicolau syndrome which is unusual in that it is associated with neuromuscular damage in a 32-year-old adult following an intramuscular injection of benzathine-penicillin into the left thigh.

CASE REPORT

A 32-year-old man with no prior history was admitted to our department with inflammatory swelling of the entire left lower limb following an intramuscular injection of 2.4 million international units of benzathine penicillin administered into the left thigh. The injection had been given ten days earlier to treat a right knee injury.

Symptoms began immediately after the injection with sudden, severe pain in the left thigh. Within hours, a purpuric lesion developed at the injection site, accompanied by partial functional impairment of the left lower limb.

The patient was reported to have taken a course in oral analgesics, the nature of which could not be specified. Three days later, pain intensity worsened, followed the next day by marked enlargement of the left lower limb, progression to complete functional impairment, and the onset of paresthesias. Two days thereafter, extensive bullous lesions appeared on the left lower limb; their subsequent rupture led to superficial ulcerations.

How to cite this article: Anderson Kouabenan AS, Gué I, Mienwoley Oussou A, Akanbi Sulé M, Koffi N'guessan W, Diabaté A. Nicolau syndrome following injection of benzathine penicillin with neurological and muscular complications. Our Dermatol Online. 2026;17(3):386-389.

Submission: 24.02.2026; **Acceptance:** 01.05.2026
DOI: 10.7241/ourd.20263.19

© Our Dermatol Online 3.2026

Dermatological examination revealed a reticulated livedo on the anterior aspect of the left thigh measuring 20 mm x 10 mm centred by a necrotic-purpuric plaque (Figs 1a and 1b), diffuse inflammatory edema involved the entire left lower limb, with ulcerations on the left leg and dorsum of the left foot secondary to ruptured bullae (Fig. 1c).

Neuromuscular assessment demonstrated truncal involvement of the left femoral nerve, manifesting as impaired active knee extension due to quadriceps weakness, while dorsiflexion of the left foot was preserved. The left patellar tendon reflex was diminished. Sensory abnormalities included hypoesthesia and dysesthesia over the anterior thigh, medial aspect of the left knee, and medial calf. Passive and active movements elicited pain along the anterior thigh, medial calf, and anterolateral leg. Additionally, there was a fixed contracture of the left thigh musculature. Peripheral pulses were palpable distally. Active and passive range of motion at the left knee was significantly restricted. The remainder of the physical examination was unremarkable. Electromyography (EMG) and nerve conduction studies (NCS) were not performed due to lack of availability at our institution.

Laboratory investigations showed elevated inflammatory and muscle injury markers: C-reactive protein (CRP) 81.25 mg/L (normal <5 mg/L), creatine phosphokinase (CPK) 1132 IU/L (normal <190 IU/L), lactate dehydrogenase (LDH) 360 IU/L (normal <250 IU/L), aspartate aminotransferase (AST) 103 IU/L, and alanine aminotransferase (ALT) 139 IU/L. Coagulation parameters were within normal limits.

Figure 1: First day: (a) Reticulated livedo on the anterior aspect of the left thigh with central necrotic purpura. (b) Reticulated livedo involving the left thigh and left knee with central necrotic purpura. (c) Inflammatory swelling of the left lower limb with overlying ulceration following bullous lesions on the left leg and dorsum of the left foot.

Arteriovenous Doppler ultrasonography of the lower limbs ruled out arterial or venous thrombosis.

The differential diagnosis included anterior compartment syndrome of the left thigh, purpura fulminans, and Nicolau syndrome. Anterior compartment syndrome was deemed unlikely due to persistent resting pain that paradoxically improved with analgesics—despite absence of fasciotomy and lack of typical exertion-related exacerbation. Purpura fulminans was excluded given the absence of systemic infection, hemodynamic instability, underlying comorbidities, and the non-progressive, localized nature of the purpuric lesions.

Based on the temporal association with intramuscular benzathine penicillin administration, characteristic reticulated livedo, femoral nerve trunk involvement, thigh muscle spasm, and elevated CPK and LDH levels, a diagnosis of Nicolau crural syndrome with neurological and muscular complications was established.

The patient was hospitalized and treated with oral amoxicillin–clavulanic acid (3 g/day), subcutaneous enoxaparin (4000 IU once daily) for thromboprophylaxis, and oral tramadol (150 mg/day) for analgesia. Local wound care included cleansing of post-bullous ulcers with igarsan foaming solution (Till ® 0.3%), followed by twice-daily application of 2% aqueous eosin and occlusive dressings with trolamine cream applied every other day to necrotic-purpuric and crusted areas. Bedside physiotherapy was initiated promptly.

Clinical improvement was observed within three days, with reduced pain intensity. Partial recovery of motor function occurred on day 7. By day 15, necrotic plaques had sloughed, leaving crusted ulcerations (Figs 2a – 2c). Laboratory parameters normalized by day 30. However, neurological deficits remained unchanged at one-month follow-up, necessitating ongoing rehabilitation.

DISCUSSION

The present case is notable for two key reasons. First, to our knowledge, this represents the first documented case of Nicolau syndrome (NS) reported in our country. Second, it features significant neuromuscular involvement of the left lower limb, including a mixed sensory-motor deficit, neuropathic pain,

Figure 2: Fifteenth day: (a) Ulcerations at the center of reticulated livedo on the anterior aspect of the thigh. (b) Ulcerations of the left thigh and left knee surrounded by a reticulated livedo. (c) Diffuse swelling of the entire left lower limb with crusted ulcerations.

quadriceps contracture, and elevated serum muscle enzymes (creatine phosphokinase (CPK) and lactate dehydrogenase (LDH).

Nicolau syndrome (NS) was first reported in 1925 following an intra-muscular injection of bismuth salt [3].

Its pathogenesis remains incompletely understood, but several hypotheses have been proposed: post-injection vasospasm mediated by sympathetic nervous system activation or arterial thrombosis or embolism secondary to intravascular crystallization of the injected drug and direct mechanical trauma to arteries or nerves from the needle itself [4]. In our patient, the most plausible mechanisms are vasospasm and direct needle injury to the left femoral nerve. Vasospasm induced ischemia, leading to cutaneous necrosis and severe pain, while direct trauma to the femoral nerve trunk explains the observed motor weakness, sensory disturbances, and quadriceps spasm.

As our patient was an adult, in the absence of contraindications, an intramuscular injection in the buttock would have been judicious, unlike one in the thigh.

The nature of the injectable drugs responsible for NS is varied (included several therapeutic classes in particular NSAIDs such as ibuprofen [5], diclofenac [6], corticoids such as methylprednisolone [7], antibiotics such as benzathine-penicillin [8]). Furthermore, NS has been reported after subcutaneous, intravenous, intramuscular, and intra-articular injections [1,2]. This would support the idea that NS is not necessarily due to the nature of the product or the mode of administration, but to the injection itself.

NS is clinically manifested by intense pain and erythema immediately after the injection, followed a few days later by the appearance of a livedoid lesion that may spread. After one to two weeks, cutaneous, subcutaneous, and/or muscular necrosis appears. Complications have been reported in the form of sensory-motor disorders (motor deficits, hypo, or anaesthesia [9]), compartment syndrome [10] and ischaemia [11]. Our patient presented nerve complications such as motor deficit in the left lower limb and dysesthesia in the left leg and foot, as well as muscle complications such as necrosis in the quadriceps with elevated CPK and LDH.

Neurological involvement in NS, though uncommon, has been previously described. For instance, intramuscular gluteal injections of benzathine penicillin have been associated with lower-limb motor deficits accompanied by urinary/fecal incontinence and hematuria [8,12]. Additionally, a case of NS following gentamicin injection into the left thigh resulted in isolated muscular injury of the lower limb [13].

NS is treated symptomatically. It includes local care with necrosectomy, combined with analgesics, antibiotic cover therapy and sometimes rehabilitation.

CONCLUSION

Nicolau syndrome is a rarely reported aetiology of cutaneous necrosis. This case underscores the critical need for high-quality training of healthcare personnel who administer intramuscular injections in adults, as well as strict adherence to established preventive measures. These include: proper identification of appropriate intramuscular injection sites in adults specifically the deltoid and gluteal regions, use of an adequately long needle (2.5–4 cm), aspiration prior to drug administration to confirm the absence of intravascular placement, application of the Z-track technique to prevent post-injection leakage of the medication into subcutaneous tissues, rotation of injection sites in cases of repeated administration and immediate cessation of the injection if the patient reports acute pain.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

REFERENCES

1. Ezzedine K, Vadoud-Seyedi J, Heenen M. Nicolau syndrome following diclofénac administration. Br J Dermatol. 2004;150 suppl 2:385-6.
2. Nischal K, Basavaraj H, Swaroop M, Agrawal D, Sathyanarayana B, Umashankar N. Nicolau syndrome: an iatrogenic cutaneous necrosis. J Cutan Aesthet Surg. 2009;2:92-5.
3. Nicolau S. Dermite livédoïde et gangréneuse de la fesseconsécutive aux injections intramusculaires dans la syphilis. A propos d'un cas d'embolie artérielle bismuthique. Ann Mal Vener. 1925;20:321-39.
4. Luton K, Garcia C, Poletti E, Koester G. Nicolau syndrome: three cases and review. Int J Dermatol. 2006;45 suppl 11:1326-8.
5. Kim SK, Kim TH, Lee KC. Nicolau syndrome after intramuscular injection: 3 cases. Arch Plast Surg. 2012;39 suppl 3:249-52.
6. Kim KK. Nicolau Syndrome in Patient Following Diclofenac Administration: a case report. Ann Dermatol. 2011;23 suppl 4:501-3.
7. Bouvy S, Fossoul S. Un syndrome de Nicolau post-injection de glucocorticoïdes. Louvain Med. 2019;138 suppl 4:199-202.
8. Elfatoiki FZ, Ennajdi A, Gueddari W, Chiheb S. Dermite livédoïde de Nicolau avec atteinte neurologique sévère chez un enfant. Ann Dermatol Venéreol. 2017;144:426-9.
9. Shelley BP, Prasad P, Manjunath MM, Chakraborti S. Hyperacute paraplegia and neurovascular (immuno vasculotoxic) catastrophe of Nicolau syndrome: primum non nocere. Ann Indian Acad Neurol. 2019;22 suppl 1:104-8.
10. Enshaei A, Afshar A. Compartment Syndrome of the Calf Due to Nicolau Syndrome. Arch Bone Jt Surg. 2016;4 suppl 1:87-9.
11. Tougouma SJB, Soulama M, Konate I, Tapsoba E, Yameogo NV, Dakoure P. Ischémie aiguë de membre sévère sanctionnée par désarticulation de sauvetage dans un contexte de syndrome de Nicolau suite à une injection intramusculaire de pénicilline: à propos d'un cas. Pan Afr Med. 2020;37:378.
12. Bharath R, Omar A, Fareed J, Naveen MAG, Gaurav G, Hai S, et al. Nicolau Syndrome, Masquerader of Postinjection Sciatic Nerve Injury: Case Report and Review of Literature. World Neurosurgery. 2020;143:51-5.
13. Kim DH, Ahn HH, Kye YC, Choi JE. Nicolau syndrome involving whole ipsilateral limb induced by intramuscular administration of gentamycin. Indian J Dermatol Venereol Leprol. 2014;80:96.

Copyright by Amond Stephen Anderson Kouabenan, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Source of Support: This article has no funding source.

Conflict of Interest: The authors have no conflict of interest to declare.